

201-15427

PCA Services, Inc.
2704 Trail Wood Drive
Durham, NC 27705

June 12, 2004

Administrator
US Environmental Protection Agency
P.O. Box 1473
Merrifield, VA 22116
Attention: Chemical Right-to-Know Program

Dear Administrator:

This letter is being sent in response to the comments generated by the EPA on the test plan and robust summaries for the Alkyl Nitriles Category. This category consists of three sponsored compounds: propionitrile (CAS No. 107-12-0), butyronitrile (CAS No. 109-74-0) and isobutyronitrile (CAS No. 78-82-0).

The EPA's comments on the original test plan are given below, with the sponsoring companies' response provided in bold type. Also in response to the EPA comments, the test plan and robust summary document for propionitrile have been appropriately revised, and are submitted along with this letter. No changes were needed on the robust summary documents for butyronitrile and isobutyronitrile; therefore the dossiers submitted earlier for these substances are still current.

First, PCA Services, Inc. would like to point out that in the Agency's "Summary of EPA Comments" one of the sponsors was incorrectly identified as the Eastman Kodak Company. This is incorrect as the two companies sponsoring this category were the Eastman Chemical Company and Solutia Inc.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided for these endpoints are adequate for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for all three members of the category for acute, genetic, and developmental toxicity endpoints and for propionitrile for repeated-dose and reproductive toxicity endpoints for the purposes of the HPV Challenge Program. Given the toxicological similarities among the three chemicals, EPA agrees with the submitters' plan to use a category approach to address data gaps for butyronitrile and isobutyronitrile for the repeated-dose and reproductive toxicity endpoints.

Genetic toxicity. Two robust summaries for mammalian cell gene mutation assay in cultured L5178Y mouse lymphoma cells exposed to propionitrile provided sufficient information to evaluate the studies. However, the submitters need to explain the positive results (both genotoxic and cytotoxic) of one of the studies (ref. # 28) that was conducted at much lower

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concentrations without exogenous metabolic activation.

Response: The test material for the mouse lymphoma test given as reference 28 was misidentified as 97% propionitrile. The test material was actually "Propionitrile Tails", which is a complex mixture that remains after the distillation of crude propionitrile and can contain as little as 50% propionitrile and as much as 2% p-nitrosophenylamine. The test material is clearly identified as "propionitrile tails" by the testing laboratory and this is confirmed by the physical description of the test material. In addition, an independent part of this report describes a mouse lymphoma test of p-nitrosophenylamine that produced positive results without metabolic activation. The test article identification numbers on the test substance container described in the laboratory report are not found on either of the two analytical reports that were attached to the study.

It is concluded that the test material in this study was a distillation residue and should not be included in the Test Plan and Robust Summaries for this category. It has been removed.

Reproductive toxicity. Adequate data are available for propionitrile; however, as functional testing was not conducted by mating treated animals of both sexes, the submitter needs to explicitly describe the results for reproductive histopathology (and testicular weights) from the 14-week repeated-dose study in the robust summaries.

Response: Separate reproductive toxicity studies were conducted and reported where treated males were functionally tested for reproductive ability with untreated females (ref 25) and treated females were functionally tested for reproductive ability with untreated males (ref 25). Our understanding is that this testing of treated rats of each sex adequately fills the reproductive endpoint and there is no need to mate treated males with treated females. We recognize, however, that there was a recovery period between treatment of the males and the sacrifice when testicular weights were recorded. Testes weight data from the 14-week studies, where there was a longer duration of treatment and no recovery period, would provide additional data regarding this endpoint.

With that in mind, the results of reproductive organ tests from the 14-week study were placed into a new summary which was placed in the "Toxicity to Reproduction, Other Studies" section of the propionitrile IUCLID document. A table of terminal testes weight data was added to this summary. In addition, the results of the histopathological examination of reproductive organs and a list of the organs were added.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees with the submitters that measured data along with predicted values are adequate for the alkyl nitriles category for the fish, invertebrate, and algae endpoints for the purposes of the HPV Challenge Program. The submitters need to address minor deficiencies in the test plan and robust summaries.

Invertebrates. The test plan (p.10) and robust summary (p.18) for the 48-hour study of propionitrile in *Daphnia magna* report a 48-hour EC50 value of 250 mg/l; however, according to the robust summary, the value corresponded to an LC50 since mortality was the endpoint evaluated. Further, the test plan describes this as "The 96-hour EC50 value..." for this test, whereas the robust summary indicates that the study was conducted for 48 hours. The submitters need to address this discrepancy.

This has been corrected in the test plan and robust summary document.

Specific Comments on the Robust Summaries

Ecological Effects

Invertebrates. In the acute toxicity test with propionitrile, the "Result" section of the robust summary (p.18) noted "Three fish exposed to ...". The word "fish" should be replaced by "daphnids."

This has been corrected.

The robust summary of the acute toxicity study with isobutyronitrile does not include an explanation for the loss of test substance. The submitters need to provide this information.

The specific basis for the loss of test material is not known.

PCA Services would like to thank the Agency for their insightful review and are pleased that the EPA concluded the category to be acceptable as well as concluding that adequate data were available for all endpoints for all three members of the category. Accordingly, the two companies consider their obligations under the HPV Challenge program complete with the submission of this revised test plan and robust summaries containing corrections for the minor errors noted above by the EPA.

Yours truly,

Rod Gerwe

Rod Gerwe, Ph.D.
President, PCA Services, Inc. (contractor)

Cc Don A. Lederer, Solutia Inc.
James A. Deyo, Eastman Chemical Company